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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/586,479	06/01/2000	Alexander C. Schmidt	15280-414000US	8296

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EXAMINER	
CHEN, STACY	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 10/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/586,479	SCHMIDT ET AL.	
	Examiner	Art Unit	
	Stacy B Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for R ply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-83* is/are pending in the application.

4a) Of the above claim(s) *68-83* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 August 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 9, 2003 has been entered.

2. Claims 1-67 are pending. Claims 68-83 are withdrawn from consideration. Upon further consideration and review of co-pending applications, the following new art rejection is applied. The Office regrets any inconvenience to Applicant.

Claim Objections

3. Claims 1 and 10 are objected to because of the following informalities: Claim1 , line 4 should read "or antigenome". Claim 10, line 2, should read "promoter-proximal". Claim 15 requires subscripts for "FHHNH". Appropriate correction is required.

Summary of the claims:

The claims are drawn to an isolated infectious human-bovine chimeric parainfluenza virus (PIV) comprising a major nucleocapsid protein (N), a nucleocapsid phosphoprotein (P), a large polymerase protein (L), and a partial or complete PIV background genome or antigenome of a human PIV or bovine PIV combined with one or more heterologous gene(s) or genome segment(s) or a different PIV of a different PIV to form a human-bovine chimeric PIV genome

or antigenome, wherein the heterologous gene(s) or genome segments(s) encodes one or more of PIV N, P, C, D, V, M, F, HN and or L protein(s) or fragment(s) thereof, and additionally (claim 3) wherein the heterologous gene(s) or genome segment(s) encodes a complete open reading frame of one or more of PIV N, P, C, D, V, M, F (a glycoprotein), HN and/or L protein(s). The heterologous gene(s) or genome segment(s) includes a heterologous regulatory element. The heterologous gene or genome segment is substituted for a counterpart gene or genome segment in a partial PIV background genome or antigenome. The gene or segment is added adjacent to or within a noncoding region of the partial or complete PIV background genome or antigenome. The gene or segment can also be added or substituted at a position corresponding to a wild-type gene order position of a counterpart gene or genome segment within the partial or complete PIV background genome or antigenome. Further, the gene or segment can be added or substituted at a position that is more promoter-proximal or promoter-distal compared to a wild-type gene order position of a counterpart gene or genome segment within the partial or complete PIV background genome or antigenome. Claims are also drawn to the chimeric PIV of claim 1, wherein the chimeric genome or antigenome comprises a partial or complete BPIV background genome or antigenome combined with one or more heterologous gene(s) or genome segment(s) from a human PIV. The HPIV genes (glycoproteins HN and/or F, or a segment encoding a cytoplasmic domain, transmembrane domain, ectodomain or immunogenic epitope thereof) are substituted for one or more counterpart genes or genome segments within the BPIV background genome or antigenome. Claim 15 is drawn to a chimeric which is rBPIV3-$F_H$$HN_H$. Claims 20-23 are drawn to a chimeric PIV wherein the chimeric genome or antigenome comprises a partial or complete human PIV background genome or antigenome combined with one or more heterologous genes

or genome segments from a bovine PIV, specifically the N protein or open reading frame represented by rHPIV3-N_B. The genome or antigenome is further modified by introduction of one or more attenuating mutations identified in a biologically derived mutant PIV or other mutant non-segmented negative stranded RNA virus, such as PIV3 JS cp45. Also claimed are specific amino acid substitutions that result in phenotypic changes and alter genes. Genes and open reading frames are deleted in whole or in part, or expression is ablated by mutations. The vector genome or antigenome is a partial or complete HPIV genome or antigenome and the heterologous pathogen is not from PIV. Also claimed is a method for stimulating the immune system comprising administering a chimeric human-bovine PIV and a physiologically acceptable carrier. Also claimed is an immunogenic composition.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-9, 11-28, 30-32, 34-55 and 58 are rejected under 35 U.S.C. 102(e) as being anticipated by Belshe *et al* (5,869,036).

Belshe teaches an isolated cp-45 hybrid virus (a derivative of HPIV-3 JS) which is suitable for use as a vaccine in humans and animals comprising nucleic acid encoding nucleocapsid protein, phosphoprotein, at least one surface antigen of a target virus, and large

polymerase protein (cols. 2-3). The target virus must have an envelope and one or more surface antigens or surface glycoproteins, such as HPIV-1, HPIV-2 and RSV. Belshe discloses that the gene sequence which encodes the surface glycoproteins of the target virus may be substituted for the corresponding sequence in the cp45 genome which codes for the HN and F proteins, to result in a chimeric genome (cols. 8-9).

Bovine RSV and cattle HPIV- are potential target viruses. Other viruses include RSV (F and G proteins), influenza, measles (HN and F protein), HIV and others (col. 8, lines 42-58). Attenuating mutations are introduced into the L segment as well as other proteins (col. 5, lines 42-67 and col. 6, lines 1-3). Belshe teaches that the cp45 genome has an amino acid substitution at Leu992 in the L protein.

Belshe says the chimeric PIV can be used in a vaccine, or immunogenic composition, comprising a physiologically acceptable carrier (column 2, lines 32-33). Therefore, the claimed invention is anticipated by Belshe.

Claim Rejections - 35 USC § 103

5. Claims 29, 33, 57 and 59-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Belshe *et al* in view of Collins *et al* (6,264,957) and Klein *et al* (WO93/14207).

The teachings of Belshe are described above. Belshe is silent on attenuating mutations stabilized by multiple nucleotide changes in a codon. Belshe is also silent on the specifics of administering the chimeric vaccine to a patient.

However, Collins teaches RSV vaccines comprising subviral particles. One would have been motivated to modify the chimeric PIV of Belshe by substituting subviral particles because it

was known in the art at the time of the invention that subviral particles are effective in vaccine compositions as taught by Collins.

Klein teaches a multimeric hybrid gene, comprising RSV (G or F protein) and HPIV (F or HN protein), and combinations of these proteins such as F proteins from both PIV3 and RSV, see pages 36-37. Klein teaches a vaccine formulated for administration intranasally. One of ordinary skill would know the dosage required to elicit an immune response and would have been motivated to make the modifications of dosage and administration in order to achieve the maximum immune response. One would also know where to add the heterologous gene segment given the well-known art of recombination and would have been motivated to incorporate the segment in such a way as to ensure its expression and stability. Belshe teaches a method of incorporating the heterologous (target gene clone) segment by ligation into the PIV clone. One of ordinary skill would also have known where and how to make attenuating mutations; lacking evidence to the contrary, the mutation at position 456 has not been given patentable weight. Applicant is invited to point to the significance of a mutation of position 456. Stabilizing the mutation by making multiple nucleotide changes in a codon specifying the mutation is well with the capabilities of one of ordinary skill, and would have been advantageous in order to ensure expression of the mutation. One would have had a reasonable expectation of success given the well known practices of foreign gene expression. Therefore, the invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Double Patenting

6. Claims 1-67 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 91, 96-117, 122-129 and 141-143 of copending Application No. 09/083,793, for reasons of record. Although the conflicting claims are not identical, they are not patentably distinct from each other because the human-bovine chimeric claimed in the instant claims is disclosed in claims 91, 96-117, 122-129 and 141-143 of copending Application No. 09/083,793, having the same proteins, mutations and combinations thereof. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-67 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 91-93, 97-100 and 102-128 of copending Application No. 09/424/628, for reasons of record. Although the conflicting claims are not identical, they are not patentably distinct from each other because the chimeric human-bovine claimed in the instant claims is disclosed in claims 91-93, 97-100 and 102-128 of copending Application No. 09/424/628, having the same proteins, mutations and combination thereof. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-67 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4, 42, 44-50, 55-61, 74, 77-79 and 81-94 of copending Application No. 09/733,692, for reasons of record. Although the conflicting claims are not identical, they are not patentably distinct from each other because the chimeric human-bovine claimed in the instant claims is disclosed in claims 1-4, 42, 44-50, 55-61,

74, 77-79 and 81-94 of copending Application No. 09/733,692, having the same proteins, mutations and combinations thereof. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

7. No claim is allowed. Claims 10 and 33 are free of the prior art.

Papers relating to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 located in Crystal Mall 1. The Fax number for Art Unit 1648 is (703) 308-4426. All Group 1600 Fax machines will be available to receive transmissions 24 hrs/day, 7 days/wk. Please note that the faxing of such papers must conform with the Notice published in the Official Gazette, 1096 OG 30, (November 15, 1989).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Stacy B. Chen, whose telephone number is (703) 308-2361. The Examiner can normally be reached on Monday through Friday from 7:30 AM-4:00 PM, (EST). If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, James C. Housel, can be reached at (703) 308-4027. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SBC

Stacy B. Chen
September 26, 2003

JAMES HOUSEL 10/1/03
SUPERVISORY PATENT EXAMINER
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